Purpose: A method to decrease the risk of rectal toxicity during prostate radiotherapy treatments consists of an implantation of a rectum spacer (RS). Nevertheless the implantation of a RS is expensive and invasive. Therefore a decision support system to identify a priori whether a specific patient would benefit from a RS would be very beneficial.
We have developed a novel method to predict the CT images with a 'virtual' RS based on a CT scan without RS. Predictions of the gain of dose, and consequently of toxicity reduction can be obtained through a validated multifactorial nomogram.
Materials/methods: A patient dataset consisting of 16 prostate cancer patients with CT imaging prior and after a gel RS implantation (SpaceOAR™ System, Augmenix Inc.) was used. The median inserted gel volume was 10.5 cc. Gel contours of the first 8 patients were used as a training set to derive the spatial deformation model of the RS.
A deformation model of the RS was build, based on overlapping volumes of RS's of different patients with a probability of >3 contour corresponded with a volume of 10 cc. From this model, a deformation field was calculated that mimics the expansion of the RS between the prostate and the rectum. The CT images of the remaining 8 patients were used to validate the virtual RS model, for this the distance between the rectum and the prostate was compared for the virtual RS and the actual RS. For one patient the dose was planned on all 3 CT's (no, real and virtual spacer) according to our clinical practice (70 Gy: 28 x 2.5 Gy). We used a validated multifactorial nomogram developed for predicting acute and late radio-induced rectal toxicities.
Results: The average minimum distances between the prostate and rectum of all 8 patients in the validation set increased with 3.7±2.4 (1SD) mm when the virtual RS was applied. For the real RS the average increase in minimum distance was 5.4±2.7 mm. The mean distances between the prostate and rectum without RS was 15.8±3.2 mm, with the virtual RS this was 19.5±3.3 mm comparable to the real RS 22.0±4.3 mm.
For one patient the planned dose on all 3 CT's is shown in the table and figure.
The virtual spacer revealed a large decrease in volume receiving more than 65 Gy, which however correlated in no significant difference of predicted late toxicity.

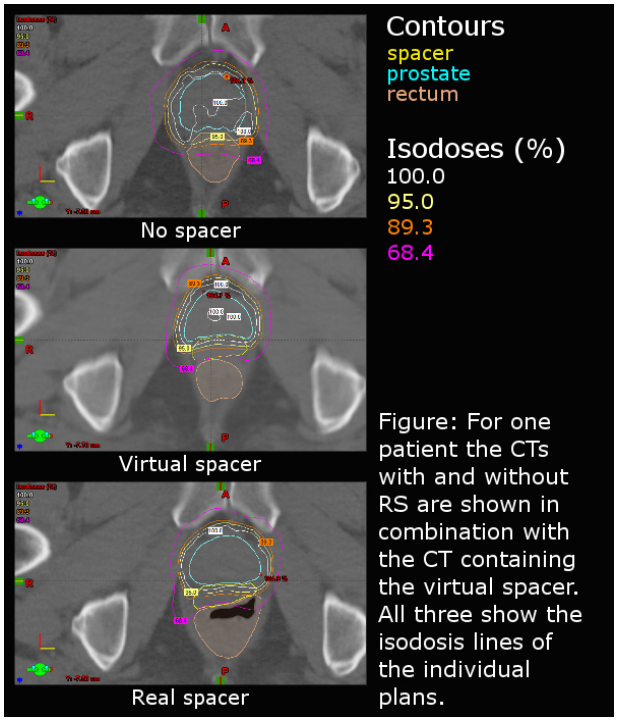

Figure: For one patient the CTs with and without RS are shown in combination with the CT containing the virtual spacer. All three show the isodosis lines of the individual plans.

Table: Planned Target Volume (PTV) coverage and dose in the organ at risk (anorectum).

	No spacer	Virtual spacer	Real spacer
PTV coverage	99.3 %	99.0 %	99.5 %
Anorectum			
V_{65}	4.3 %	1.0 %	3.3 %
D_{max}	69.1 Gy	69.7 Gy	70.5 Gy

Conclusions: We have developed a novel method to simulate a prostate-rectum spacer that is a useful tool to identify patients with a potential dose and outcome benefit of a RS implantation. The volume of the virtual RS can be estimated through the use of different deformation fields. For the presented patient the RS would not give a clinical benefit, so this patient should not get a RS. We envision that in the future this virtual spacer-based decision support system will be used to quantify a priori the potential benefit of such approach, more particularly before extremely hypofractionated schedules.

Keywords: Prostate Cancer – Rectum Spacer – Virtual Spacer – Predicted Gain

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The use of ^{149}Tb and ^{152}Tb in preclinical investigations: an update on its mass separation and subsequent application for imaging and therapy

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Purpose: Terbium is a unique element as it provides a quadruplet of radionuclides suited for diagnostics and therapy in nuclear medicine [1]. As part of the PSI-ISOLDE collaboration, we concentrated on the collection and purification of ^{149}Tb (α-emitter, $T_{1/2}$ = 4.1 h – for potential therapy) and ^{152}Tb (β^+-emitter, $T_{1/2}$ = 17.5 h – for use in PET imaging), for significant imaging and therapy investigations.
Materials/methods: Mass-separated beams of ^{149}Tb and ^{152}Tb, respectively, were implanted at ISOLDE-CERN into Zn-coated Au foils. With 1.5 hours of collection and 2 hours decay of co-implanted activities, up to 200 MBq ^{149}Tb could be transported to PSI. Collections of ^{152}Tb lasted 4 to 6 hours and up to 2 GBq ^{152}Tb could be shipped to PSI.
The Tb radionuclides were extracted from the Zn foils by dissolving them in HNO_3/NH_4NO_3, loaded on to a macroporous strongly acidic cation exchange resin and the Tb radionuclides eluted using dilute α-hydroxyisobutyric acid (α-HIBA). The product eluent was used directly for the radiolabeling process.
Complementing previous therapy studies with ^{149}Tb-folate and ^{161}Tb-folate [2, 3], we focused on the possible side effects of such a treatment. Healthy mice, without tumors, were injected with increasing activity levels to investigate kidney damage after α-therapy with ^{149}Tb-folate and compare it with the damage caused by ^{161}Tb-folate-based ß-therapy. These mice are monitored with regard to potential undesired side effects. DOTANOC and DOTA-RGD were also labelled with ^{152}Tb, a radionuclide which can potentially be used for PET imaging. They were injected into AR42J and U87MG tumor-bearing mice, which were imaged using a benchtop small animal PET/CT scanner (Genisys8, Sofie Biosciences).
Results: The ^{149}Tb and ^{152}Tb were effectively separated from Ce, Pr, Ba and La, yielding a radionuclidically pure product. The product in question was successfully labelled to DOTANOC and DOTA-RGD at high specific activity of up to 10 MBq/nmol and radiochemical purity of >95%. The ^{149}Tb-folate dose escalation study was conducted with six mice injected

with 5 MBq/mouse and three untreated controls which were injected with α-HIBA only. No impairment of animal kidney function was observed to date.
Tumor visualization was readily achieved with both ^{152}Tb-labeled peptides and, due to the high sensitivity of this scanner, it was possible to also image the tumors at late time points after injection of the mice.
Conclusion: The latest run of experiments in the PSI/ISOLDE collaboration proved to be the most successful to date, with reproducible harvesting of ^{149}Tb and ^{152}Tb and its subsequent chemical separation from impurities. The product was successfully labelled to peptides and folate and injected into mice for imaging and long-term studies to determine kidney damage, in the case of ^{149}Tb. Following these encouraging results, more ambitious studies are planned in future.

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Is dual energy CT the next standard imaging modality for radiotherapy?
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Over the past years, dual energy CT (DECT) scanners have been installed in many radiology departments. Recently, also possibilities are under investigation to use this equipment for radiotherapy purposes. Several strategies using DECT imaging may allow optimization of radiation treatment in a variety of fields: e.g. tumour detection and characterization, improved dose calculation accuracy, objective normal tissue function quantification. DECT allows a robust way of material characterization that easily can quantify the electron density and effective atomic number. These approaches improve radiotherapy dose calculation accuracy. Especially in brachytherapy and proton therapy this is necessary due to the larger uncertainties in dose calculation compared to high energy photon treatments. Other possible applications involve advanced metal artifact reduction techniques. The use of iodinated contrast material allows an objective quantification for quantitative assessment of perfusion of tumours and normal tissues. Future perspectives for DECT for radiotherapy will be discussed together with the next steps for implementation in clinical practice.

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Can we replace high quality simulation CT by simple kV-cone-beam CT images to extract an externally validated radiomics signature?
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Objective: A validated CT-based radiomic signature showed to have prognostic information for lung cancer patients[1,2]. The prognostic value of radiomic image features derived from cone-beam CT (CBCT) images has not yet been described. Furthermore, due to the fact that a CBCT image is acquired prior to each fraction it has the potential to monitor response to treatment. The goal of this study was to investigate the stability and correlation between features of the radiomic signature derived from planning CT vs. kV-CBCT and between CBCTs of different fractions.
Material/Methods: A total of 26 stage II-III NSCLC patients who received radiation therapy were included in this study. The planning CT (CT1), the CBCT prior to the first (CBCT-FX1) and second fraction (CBCT-FX2) were used in this study (see Figure). CBCT images were registered to CT1 using an automatic rigid registration prior to feature extraction. The prognostic radiomic signature[1] consists of four features: I) tumor intensity: 'Energy', II) texture: 'Grey Level Nonuniformity, III) wavelet: 'Grey Level Nonuniformity HLH' and IV) shape: 'Compactness'. Since a rigid registration was used without redelineation, the fourth feature 'Compactness' was not analyzed since no changes were performed to the shape. For the remaining three features, the correlation between feature values derived from (1) CT1 and CBCT-FX1 and (2) CBCT-FX1 and CBCT-FX2 were analyzed. Correlations were calculated using an intraclass correlation coefficient ICC(2,1).

A B

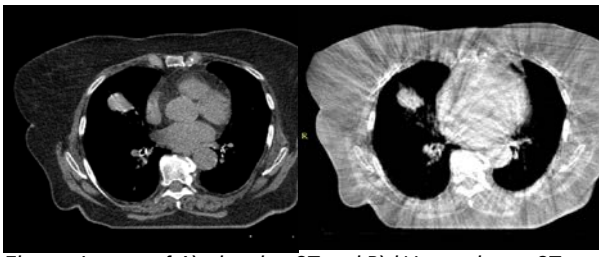

Figure: Images of A) planning CT and B) kV-cone-beam CT

Results: All three features of the radiomic signature I) 'Energy', II) 'Grey Level Nonuniformity and III) 'Grey Level Nonuniformity HLH' showed correlation of ICC>0.8 between CT1 and CBCT-FX1 (ICC = 0.98, 0.88 and 0.81 respectively) and between CBCT-FX1 and CBCT-FX2 (ICC = 0.89, 0.83 and 0.95 respectively).
Conclusion: Three features that previously showed to have prognostic performance in lung and head & neck cancer patients for CT images show a correlation above 0.8 between CT1 and CBCT-FX1. The features also show an ICC>0.8 for CBCT-FX1 vs. CBCT-FX2, which suggests stability of those features using CBCT imaging. These results show the potential of CBCT imaging in monitoring treatment and acquiring prognostic and predictive information. In the future, radiomic features derived from CBCT images will be investigated to monitor changes of CBCT features over the course of treatment (the so-called "Delta-radiomics" approach) and to evaluate its prognostic significance.

Keywords: radiomics, cone-beam computed tomography

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PET-ToF system with highly integrated SiPM readout
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SiPMs allow a dramatic improvement of PET performance. The good timing performance of SiPMs will result in better Time Of Flight time resolution, and therefore in better effective sensitivity. The small and independent photodetector pixels allow using one-to-one coupling between a SiPM pixels and a LYSO crystals. This will result in significant improvement of the spatial resolution compared to PMT base systems. To take advantage of SiPMs in PET applications, it is mandatory to have highly integrated electronics readout.
The present work expands the research in SiPM-based PET-ToF pursued by the authors since several years, in particular developing the TOFPET readout ASIC, a 64 channel mixed-